UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,328	12/07/1999	KUBER T. SAMPATH	CIBT-P01-514	9813

28120 7590 09/21/2006

FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
ROMEO, DAVID S	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 09/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/445,328	SAMPATH ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5,6,8,9,11,12,14-38 and 53-65* is/are pending in the application.

4a) Of the above claim(s) *21,22,25 and 28-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,5,6,8,9,11,12,14-20,23,24,26,27,35-38 and 53-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *2,5,6,8,9,11,12,14-38 and 53-65* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 07/03/2006 has been entered. Claims 2, 5, 6, 8, 9, 11, 12, 14–38 and 53–65 are pending. Applicant's election with traverse of Group X, the species OP-1, the species the mature form of OP-1, the species pre-renal causes of acute renal failure, the species decreased cardiac output, and the species intravenous administration in the paper mailed 08/06/2002 is acknowledged. Claims 21, 22, 25 and 28-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and/or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the paper mailed 08/06/2002.

Applicant's election of GFR in the reply filed on 03/01/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 2, 5, 6, 8, 9, 11, 12, 14-20, 23, 24, 26, 27, 35–38 and 53–65 are being examined only to the extent they read upon the elected invention and/or species.

Maintained Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 103

Claims 2, 5, 6, 8, 9, 11, 12, 14, 23, 24, 26, 27, 35, 36, 37, 38, 53, 56, 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kelly (J Clin Invest. 1996 Feb 15;97(4):1056-63) in view of Kuberasampath (WO 93/04692) and Lefer (J Mol Cell Cardiol. 1992 Jun;24(6):585-93).

Claims 2, 15-20, 53, 54, 55, 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kelly (J Clin Invest. 1996 Feb 15;97(4):1056-63) in view of Kuberasampath

(WO 93/04692) and Lefer (J Mol Cell Cardiol. 1992 Jun;24(6):585-93) as applied to claims 2, 53 above, and further in view of Anderson (Chapter 275, in Harrison's Principles Of Internal Medicine, 1980) and Brady (Chapter 236, in Harrison's Principles Of Internal Medicine, 1994). The rejection of record is applied to claims 60–65.

Insofar as the prior art teaches the prevention and treatment of acute renal failure by administering OP-1, then the differences between the teachings of the references relied upon and the limitations of claims 60–65 would have been obvious absent any evidence that these differences are unexpected and unobvious. These differences are obvious because one of ordinary skill in the art would be motivated to treat and prevent the acute renal failure.

Further with respect to claim 63, it is noted that Brady teaches that a rise in serum creatine of greater than 3 mg/dL is associated with a poor prognosis and probably reflects the extent of renal parenchymal damage and severity of the underlying disease (page 1274, paragraph bridging left and right columns).

Further with respect to claim 64, the specification discloses:

> That is, the subjects for treatment are expected to be otherwise free of indications for morphogen treatment. In some number of cases, however, the subjects may present with other symptoms (e.g., osteodystrophy) for which morphogen treatment would be indicated. Paragraph bridging pages 11-12.

The examiner uses the specification as dictionary for a definition of subjects for treatment. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to treat a mammal afflicted with acute renal failure by administering OP-1, wherein the mammal presents with osteodystrophy, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because one of ordinary skill in the art would be motivated to treat the acute renal failure.

The invention is prima facie obvious over the prior art.

Applicants argue that a reasonable expectation of success is lacking because applicants have proven that antiinflammatory properties are not sufficient to treat ARF and that antiinflammatory agents have detrimental effects on renal function. Applicants' arguments have been fully considered but they are not persuasive. The fact that agents designed to block leukocyte-endothelial interactions mediated via ICAM-1 may be therapeutically effective in the prevention and treatment of acute renal failure (Kelly, page 1062, left column, full paragraph 2) and that Kuberasampath and Lefer teach that OP-1 is an agent that exhibits significant anti-adherent actions on PMNs provides one of ordinary skill in the art with at least a reasonable expectation of success. Applicants are conflating antiinflammatory properties of the antiinflammatory agents TGF-β1, CsA, and NSAIDs with detrimental effects of TGF-β1, CsA, and NSAIDs on renal function. There is no evidence of record that OP-1 possesses any of the detrimental renal side-effects of TGF-β1, CsA, or NSAIDs or that one skilled in the art would have expected OP-1 to possess any of the detrimental renal side-effects of TGF-β1, CsA, or NSAIDs. Therefore, Applicants' arguments are insufficient to rebut the *prima facie* case of obviousness.

Applicants argue that the examiner has failed to examine the elected species pre-renal causes of ARF because the rejection only relates to using OP-1 to treat ARF caused by renal ischemia and because renal ischemia is not a pre-renal cause of ARF. Applicants' arguments have been fully considered but they are not persuasive.

The examiner made specific findings as to the elected species decreased cardiac output in the Office action mailed 07/12/2004 at page 10, last full paragraph and paragraph bridging pages 10-11.

Reciting "mammal is afflicted with acute renal failure caused by a pre-renal cause" (claim 20), or "the acute renal failure being one arising from a pre-renal cause" (claim 58) does not exclude kidney tissue damage because Brady (Exhibit A, 11/17/2005) teaches that severe or prolonged hypoperfusion may lead to ischemic renal parenchymal injury and intrinsic renal azotemia (page 1266, left column, full paragraph 2). Furthermore, the specification (page 1, lines 21-25) recognizes that "Pre-renal causes ... may lead to significant permanent and/or progressive damage to renal tissues." In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "not for treating a mammal with renal damage caused by continued pre-renal causes of ARF) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

As previously indicated, Kelly (page 1062, left column, full paragraph 2) teaches that agents designed to block leukocyte-endothelial interactions mediated via ICAM-1 may be therapeutically effective in the prevention and treatment of acute renal failure. Prevention and treatment of acute renal failure, as taught by Kelly, teaches, suggests, or motivates treatment of a mammal afflicted with acute renal failure caused by decreased cardiac output because severe or prolonged hypoperfusion may lead to ischemic renal parenchymal injury and intrinsic renal azotemia. One of ordinary skill in the art would be motivated to make this modification because

impaired cardiac output is a major cause of acute deterioration in renal function and the management of acute renal failure should focus on elimination of the causative hemodynamic abnormality or toxin, avoidance of additional insults, and prevention and treatment of complications.

The outstanding grounds of rejection in this final rejection have been reiterated and the examiner believes that all grounds of rejection have been sufficiently clearly developed to such an extent that applicants may readily judge the advisability of an appeal. Regarding claims 58 and 59, these claims were clearly rejected in the last Office action and the rejection was reiterated in the present Office action. The examiner made specific findings as to the elected species decreased cardiac output in the Office action mailed 07/12/2004 at page 10, last full paragraph and paragraph bridging pages 10-11. The examiner made specific findings regarding an improvement in a standard marker of renal function in the Office action mailed 05/17/2005 at paragraph bridging pages 6-7. Prior to the claim amendments that necessitated the rejection of 05/17/2005, this limitation only limited the properties of the agent administered and did not limit the method. See the Office action mailed 07/12/2004 at paragraph bridging pages 9-10 and the restriction mailed 02/01/2005.

New Formal Matters, Objections, and/or Rejections:

Claim Objections

Claim 63 is objected to because of the following informalities: "100/mg/dL/day" should be "100 mg/dL/day". Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 60–61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "frequently" in claim 60 is a relative term which renders the claim indefinite. The term "frequently" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. Claim 61 depends on claim 60 and also shares its deficiency.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 9:00 A.M. TO 5:30 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING MAY BE OBTAINED FROM THE PATENT APPLICATION INFORMATION RETRIEVAL (PAIR) SYSTEM. STATUS INFORMATION FOR PUBLISHED APPLICATIONS MAY BE OBTAINED FROM EITHER PRIVATE PAIR OR PUBLIC PAIR. STATUS INFORMATION FOR UNPUBLISHED APPLICATIONS IS AVAILABLE THROUGH PRIVATE PAIR ONLY. FOR MORE INFORMATION ABOUT THE PAIR SYSTEM, SEE HTTP://PAIR-DIRECT.USPTO.GOV. CONTACT THE ELECTRONIC BUSINESS CENTER (EBC) AT 866-217-9197 (TOLL-FREE) FOR QUESTIONS ON ACCESS TO THE PRIVATE PAIR SYSTEM,

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
SEPTEMBER 17, 2006